CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, Nov. 2002, p. 1401 Vol. 9, No. 6
1071-412X/02/$04.00+0 DOI: 10.1128/CDLI.9.6.1401.2002

Interleukin-8 (IL-8) Preferable to IL-6 as a Marker for Clinical Infection

Concentrations of cytokines such as interleukin-6 (IL-6) and IL-8 in serum have been studied as diagnostic markers for neonatal bacterial infection (1–4, 6, 7). In a recent study by Krueger et al., a random-access chemiluminescence assay, Immulite, was used to show that the diagnosis of early-onset infections in neonates can be established or ruled out with a high level of confidence by measuring IL-6 or IL-8 levels in cord blood (6). However, when values of IL-6 and IL-8 are determined with this method, the required plasma volume and assay time are twice as high for IL-6 (0.1 ml, 70 min) as for IL-8 (0.05 ml, 40 min), according to the manufacturer's instructions. The aim of our study was to evaluate the correlation of IL-6 and IL-8 values during neonatal clinical infection (CI) and to assess whether IL-8 would be a more beneficial infection marker, especially in preterm neonatal intensive care unit (NICU) patients, since IL-8 determinations are more rapid and require less sample volume.

We determined levels of IL-6 and IL-8 (Immulite System; DPC Biermann, Bad Nauheim, Germany) in plasma from 100 consecutive preterm and term infants admitted to our NICU. These levels were analyzed prospectively in umbilical cord blood samples of all infants directly after birth (100 samples). Repeat samples from the same infants were also obtained when clinical signs of infection developed or to assess the effectiveness of antimicrobial therapy (117 samples). Patients who underwent surgery were excluded from the study. For classification of IL-6 and IL-8 values as positive or negative, cutoff levels of >100 pg/ml for IL-6 (6) and >70 pg/ml for IL-8 (3) were used. All patients with discordant IL-6 or IL-8 results were retrospectively assessed for evidence of CI. We diagnosed CI in the presence of at least one clinical sign compatible with CI (5) and a C-reactive protein level of >5 mg/liter within 24 h before or after IL-6 or IL-8 determination.

There was a significant overall correlation between the IL-6 and IL-8 values ($r = 0.50$, $P < 0.001$). The P value from McNemar's test for agreement was 0.24, and the kappa coefficient was 0.59 (95% confidence interval [CI] = 0.47 to 0.71). Overall, 182 samples (83.9%) from 77 patients were concordant, meaning that both cytokines were either below or above the respective cutoff value. Thirty-five samples (16.1%) from 23 patients were discordant in this respect. Of these 23 patients, 8 (34.8%) suffered from CI. Of the 13 samples from eight patients with infection, false-negative results for IL-6 were found in seven samples from five patients and for IL-8 in six samples from four patients. Of the 22 discordant samples from 16 infants without infection, 15 samples from 11 patients demonstrated false-positive IL-6 values but only seven samples from seven infants showed false-positive IL-8 values. For the discordant group, there was no statistically significant difference in sensitivity ($P = 1.0$) and specificity ($P = 0.134$) for CI between the two cytokines. The negative predictive values for all 217 sample sets were 82.4% for IL-6 and 82.1% for IL-8. The positive predictive values for IL-6 and IL-8 were 79.3 and 80.0%, respectively. The differences between the positive and negative predictive values for IL-6 and IL-8 were not statistically significant ($P > 0.5$).

In conclusion, IL-6 and IL-8 levels in plasma correlated well and did not show a significant difference in sensitivity and specificity for CI. IL-8 would be a more useful infection marker especially in preterm NICU patients, since IL-8 determinations are more rapid and require less sample volume.

REFERENCES

1. **Buck, C., J. Bundschu, H. Gallati, P. Bartmann, and F. Pohlandt.** 1994. Interleukin-6: a sensitive parameter for the early diagnosis of neonatal bacterial infection. Pediatrics **93:**54–58.
2. **Doellner, H., K. J. Arntzen, P. E. Haereid, S. Aag, and R. Austgulen.** 1998. Interleukin-6 concentrations in neonates evaluated for sepsis. J. Pediatr. **132:** 295–299.
3. **Franz, A. R., M. Kron, F. Pohlandt, and G. Steinbach.** 1999. Comparison of procalcitonin with interleukin 8, C-reactive protein and differential white blood cell count for the early diagnosis of bacterial infections in newborn infants. Pediatr. Infect. Dis. J. **18:**666–671.
4. **Franz, A. R., G. Steinbach, M. Kron, and F. Pohlandt.** 1999. Reduction of unnecessary antibiotic therapy in newborn infants using interleukin-8 and C-reactive protein as markers of bacterial infections. Pediatrics **104:**447–453.
5. **Klein, J. O.** 2001. Bacterial sepsis and meningitis, p. 943–998. *In* J. S. Remington and J. O. Klein (ed.), Infectious diseases of the fetus and newborn infant, 5th ed. The W. B. Saunders Company, Philadelphia, Pa.
6. **Krueger, M., M. S. Nauck, S. Sang, R. Hentschel, H. Wieland, and R. Berner.** 2001. Cord blood levels of interleukin-6 and interleukin-8 for the immediate diagnosis of early-onset infection in premature infants. Biol. Neonate **80:**118–123.
7. **Messer, J., D. Eyer, L. Donato, H. Gallati, J. Matis, and U. Simeoni.** 1996. Evaluation of interleukin-6 and soluble receptors of tumor necrosis factor for early diagnosis of neonatal infection. J. Pediatr. **129:**574–580.

Joern-Hendrik Weitkamp*
Jochen Reinsberg
Peter Bartmann
Department of Neonatology
Centers for Pediatrics, Obstetrics and Gynecology
University of Bonn
D-53113 Bonn, Germany

*Phone: 615-322-2250
Fax: 615-343-9723
E-mail: hendrik.weitkamp@vanderbilt.edu